

WHAT IS CLAIMED IS:

1 1. A microfluidic device for treating a particle comprising:
2 (a) an input mechanism for introducing a fluid sample containing a particle;
3 (b) a microfluidic passage in fluid communication with said input mechanism;
4 (c) a positioning mechanism in fluid communication with said microfluidic
5 passage, said positioning mechanism for positioning said particle in said
6 microfluidic passage while contained in said fluid sample;
7 (d) a retention mechanism for retaining said particle upon being positioned by
8 said positioning means;
9 (e) a treatment mechanism in communication with said retention mechanism for
10 selectively treating said particle to produce a treatment response while being
11 retained within said retention mechanism; and,
12 (f) a measurement mechanism for measuring said treatment response, if any, of
13 said particle.

1 2. The microfluidic device of claim 1 further comprising a release mechanism for
2 releasing said particle from said retention mechanism.

1 3. The microfluidic device of claim 2 further comprising an output mechanism for
2 outputting said particle from said microfluidic device.

1 4. The microfluidic device of claim 2 further comprising a cell culture mechanism for
2 culturing said particle.

1 5. The microfluidic device of claim 1 further comprising a control mechanism for
2 determining aspects of the flow rate or path of the sample fluid or other fluid.

1 6. The microfluidic device of claim 5, wherein said control mechanism is a valve in
2 communication with said microfluidic passage.

1 7. The microfluidic device of claim 6, wherein said microfluidic device is formed from a
2 multi-layer elastomeric block and, wherein said valve is formed from an elastomeric
3 membrane within said elastomeric block.

1 8. The microfluidic device of claim 6, wherein said control mechanism is a pump in
2 communication with said microfluidic passage.

1 9. The microfluidic device of claim 8, wherein said microfluidic device is formed from a
2 multi-layer elastomeric block and, wherein said pump is formed from an elastomeric
3 membrane within said elastomeric block.

1 10. The microfluidic device of claim 1, wherein said microfluidic device comprises a
2 multi-layered elastomeric block having a control layer having an elastomeric membrane
3 deflectable into said microfluidic passage in a fluidic layer to determine the flow rate or path
4 of a fluid in said microfluidic passage.

1 11. The microfluidic device of claim 1, wherein said microfluidic device comprises a
2 layer including a material selected from the group consisting of elastomers,
3 polydimethylsiloxane, plastic, polystyrene, polypropylene, polycarbonate, glass, ceramic,
4 silicon, sol-gels, metal, metalloids, metal oxides, biological polymers, mixtures thereof,
5 particles, proteins, gelatins, polylysine, serum albumin, collagen, nucleic acids, and
6 microorganisms.

1 12. The microfluidic device of claim 1, wherein said microfluidic passage has is less than
2 about 500 micrometers wide.

1 13. The microfluidic device of claim 1, wherein said microfluidic passage further
2 comprises an adjacent passage joining said microfluidic passage at a junction or branch, said
3 adjacent passage being selected from the group consisting of inlet passage, outlet passage,
4 particle passage, reagent passage, and waste passage.

1 14. The microfluidic device of claim 13, wherein said adjacent passage is a dead-end
2 passage.

1 15. The microfluidic device of claim 13 further comprising said adjacent passage
2 manipulating said particle.

1 16. The microfluidic device of claim 15, wherein said particle manipulating is selected
2 from the group of positioning, sorting, retaining, treating, detecting, propagating, storing,
3 mixing, and releasing.

1 17. The microfluidic device of claim 1, wherein said particle is selected from the group
2 consisting of cells, eukaryotic cells, prokaryotic cells, plant cells, animal cells, hybridoma
3 cells, bacterial cells, yeast cells, viruses, organelles, beads, and vesicles.

1 18. The microfluidic device of claim 17, wherein said particle is a plurality or an
2 aggregate of particles.

1 19. The microfluidic device of claim 18, wherein said plurality of particles is a complex
2 mixture containing different particles.

1 20. The microfluidic device of claim 19, wherein said complex mixture containing
2 different particles is whole blood or serum or bodily fluid.

1 21. The microfluidic device of claim 1, wherein said particle is an egg or embryo.

1 22. The microfluidic device of claim 1, wherein the input mechanism is a receptacle or
2 well in fluid communication with said microfluidic passage.

1 23. The microfluidic device of claim 22, wherein the input mechanism has a volume
2 greater than a volume defined by said microfluidic passage.

1 24. The microfluidic device of claim 1 further comprising a facilitating mechanism in
2 communication with or acting upon said input mechanism.

1 25. The microfluidic device of claim 24, wherein said facilitating mechanism is selected
2 from the group consisting of gravity, fluid pressure, centrifugal pressure, pump pressure, and
3 negative fluid pressure.

1 26. The microfluidic device of claim 1, wherein said positioning mechanism is a direct
2 positioning mechanism or an indirect positioning mechanism.

1 27. The microfluidic device of claim 26, wherein said direct positioning mechanism is a
2 force selected from the group consisting of optical, electrical, magnetic, and gravitational.

1 28. The microfluidic device of claim 27, wherein said electrical force is selected from the
2 group consisting of electrophoretic, electroosmotic, electroendoosmotic, and
3 dielectrophoretic.

- 1 29. The microfluidic device of claim 26, wherein said indirect positioning mechanism is a
2 longitudinal indirect positioning mechanism or a transverse indirect positioning mechanism.
- 1 30. The microfluidic device of claim 29, wherein said indirect positioning mechanism is
2 facilitated by a pump or a valve associated with said microfluidic device.
- 1 31. The microfluidic device of claim 29, wherein said transverse indirect positioning
2 mechanism is facilitated by a fluid flow stream at a passage junction, laterally disposed
3 region of reduced fluid flow, or channel bend.
- 1 32. The microfluidic device of claim 31, wherein said passage junction is unifying or
2 dividing.
- 1 33. The microfluidic device of claim 29, wherein said transverse indirect positioning
2 mechanism is a laminar flow-based transverse positioning means.
- 1 34. The microfluidic device of claim 29, wherein said transverse indirect positioning
2 mechanism is a stochastic transverse positioning mechanism.
- 1 35. The microfluidic device of claim 34, wherein said stochastic transverse positioning
2 mechanism randomly selects said particle from a population of particles by lateral separation
3 of said particle in said sample fluid from a main flow region to a reduced flow region.
- 1 36. The microfluidic device of claim 29, wherein said transverse indirect positioning
2 mechanism is a centrifugal forced-based transverse positioning mechanism.
- 1 37. The microfluidic device of claim 1 wherein said retention mechanism selectively
2 retains said particle at a pre-selected region within said microfluidic device.
- 1 38. The microfluidic device of claim 37, wherein said retention mechanism retains said
2 particle by overcoming or counteracting a force caused by said positioning mechanism.
- 1 39. The microfluidic device of claim 1, wherein said retention mechanism is a trap or
2 barrier-based retention mechanism.
- 1 40. The microfluidic device of claim 39, wherein said barrier-based retention mechanism
2 restricts longitudinal movement of said particle in or adjacent said microfluidic passage.

- 1 41. The microfluidic device of claim 38, wherein said retention mechanism is a protrusion
2 extending, fixedly or transiently, into or adjacent said microfluidic passage to restrict
3 longitudinal movement of said particle.
- 1 42. The microfluidic device of claim 26, wherein said direct positioning mechanism is a
2 chemical retention mechanism.
- 1 43. The microfluidic device of claim 42, wherein said chemical retention mechanism is
2 based on a specific affinity between said particle and said retention mechanism.
- 1 44. The microfluidic device of claim 1, wherein said treatment mechanism is a fluid-
2 mediated mechanism or a non-fluid mediated mechanism.
- 1 45. The microfluidic device of claim 1, wherein said treatment mechanism exposes said
2 particle to a reagent or physical condition.
- 1 46. The microfluidic device of claim 45, wherein said reagent is selected from the group
2 consisting of chemical modulator, biological modulator, agonist, antagonist, hormone, ligand,
3 small molecule, peptide, protein, carbohydrate, lipid, receptor, nutrient, toxin, drug, chemical
4 substance, compound, ion, polymer, nucleic acid, material, complex, mixture, aggregate, dye,
5 stain, fluorescent dye, detection agent, assay agent, substrate, substrate inhibitor, antibody,
6 labeled substance, and biological particle.
- 1 47. The microfluidic device of claim 46, wherein said reagent attracts or repels said
2 particles.
- 1 48. The microfluidic device of claim 45, wherein said reagent induces or inhibits cell
2 particle proliferation.
- 1 49. The microfluidic device of claim 45, wherein said reagent is cytotoxic.
- 1 50. The microfluidic device of claim 44, wherein said fluid-mediated mechanism further
2 comprises a fluid treatment and wherein said particles are introduced to said fluid treatment.
- 1 51. The microfluidic device of claim 44, wherein said fluid-mediated mechanism
2 functions in conjunction with the functioning of said positioning mechanism.

- 1 52. The microfluidic device of claim 51, wherein said positioning mechanism is a
2 transverse positioning mechanism for moving said particle into and out of said fluid-mediated
3 mechanism to modulate exposure of said particle to said treatment fluid.
- 1 53. The microfluidic device of claim 45, wherein said physical condition is selected from
2 the group consisting of heat, light, radiation, sub-atomic particles, electric fields, magnetic
3 fields, pressure, acoustical pressure, gravity, and micro-gravity.
- 1 54. The microfluidic device of claim 1, wherein said measurement mechanism is a
2 detector associated with said microfluidic device that detects a characteristic of said particle
3 or caused by said particle.
- 1 55. The microfluidic device of claim 54, wherein said detector is selected from the group
2 consisting of spectrometers, electronic sensors, hydrodynamic sensors, imaging systems, and
3 photon detectors.
- 1 56. The microfluidic device of claim 54, wherein said detector detects multiple values.
- 1 57. The microfluidic device of claim 54, wherein said detector employs a detection mode
2 that is selected from the group consisting of time-independent, time-dependent, and averaged.
- 1 58. The microfluidic device of claim 54, wherein said detector is a spectroscopic detector
2 that detects a signal produced of a type selected from the group consisting of absorption,
3 luminescence, photoluminescence, chemiluminescence, electroluminescence, magnetic
4 resonance, nuclear resonance, electron spin resonance, scattering, electron scattering, light
5 scattering, neutron scattering, diffraction, circular dichroism, optical rotation, fluorescence
6 intensity, fluorescence resonance energy transfer, fluorescence polarization, fluorescence
7 lifetime, total internal reflection fluorescence, fluorescence correlation spectroscopy,
8 fluorescence recovery after photobleaching, fluorescence activated cell sorting, and
9 phosphorescent.
- 1 59. The microfluidic device of claim 54, wherein said detector is an electrical detector
2 capable of detecting a signal selected from the group consisting of current, voltage,
3 resistance, capacitance, and power.

1 60. The microfluidic device of claim 54, wherein said detector is a hydrodynamic detector
2 which detects a hydrodynamic interaction between said particle and a fluid, another particle,
3 or said microfluidic passage.

1 61. The microfluidic device of claim 60, wherein said interaction included a
2 hydrodynamic interaction selected from the group consisting of chromatography,
3 sedimentation, viscometry, electrophoresis.

1 62. The microfluidic device of claim 54, wherein said detector is an imaging detector for
2 creating and analyzing images of said particle(s).

1 63. The microfluidic device of claim 54, wherein said detector detects a biological
2 response produced by said particle(s).

1 64. The microfluidic device of claim 63, wherein said biological response is selected from
2 the group consisting of chemotaxis, biotaxis, senescence, apoptosis, proliferation,
3 differentiation, morphological change, pH change, and calcium uptake.

1 65. The microfluidic device of claim 1, further comprising a detection site, wherein said
2 particle or product of said particle, is detected by said detector.

1 66. The microfluidic device of claim 65, wherein said detection site is within said
2 microfluidic device.

1 67. The microfluidic device of claim 65, wherein said detection site is located external to
2 said microfluidic device.

1 68. The microfluidic device of claim 54, wherein said detector detects a characteristic of
2 said particle, directly or indirectly, said characteristic being selected from the group
3 consisting of particle identity, particle number, particle concentration, composition, structure,
4 sequence, activity, molecular character, morphology, phenotype, genotype, growth,
5 apoptosis, necrosis, lysis, alive/dead ratio, position in cell cycle, activity of signal pathway,
6 differentiation, transcriptional activity, substrate attachment, cell-cell interaction,
7 translational activity, replication activity, transformation, heat shock response, motility,
8 spreading, membrane integrity, chemotaxis, and neurite outgrowth.

1 69. The microfluidic device of claim 2, wherein said release mechanism operates by
2 removing a retaining force caused by said retaining mechanism.

1 70. The microfluidic device of claim 2, wherein said release mechanism operates by
2 overcoming a retaining force caused by said retaining mechanism.

1 71. The microfluidic device of claim 2, wherein said release mechanism operates by
2 rendering ineffective a retaining force caused by said retaining mechanism.

1 72. The microfluidic device of claim 2, further comprising directing said particle to
2 another region within or external said microfluidic device.

1 73. The microfluidic device of claim 72, wherein said another region is selected from the
2 group consisting of a second positioning mechanism, a second detection mechanism, a
3 second retention mechanism, and an output mechanism.

1 74. The microfluidic device of claim 73, wherein said second retention mechanism is a
2 cell culture chamber.

1 75. The microfluidic device of claim 3, further comprising said output mechanism
2 outputting said particle to a location selected from the group consisting of an internal sink,
3 and external sink, a waste site, a collection site, a cell growth chamber, and an external cell
4 culture plate.

1 76. A method for perfusing cells with a reagent comprising the steps of:

2 (a) providing a microfluidic device having

3 (i) a cell growth chamber,

4 a cell inlet in communication with said chamber, said cell inlet having an in
5 valve in operable communication therewith to valve fluid flow through said
6 cell inlet into said chamber, wherein said cells can pass through said cell inlet
7 into said chamber when said inlet valve is open, but cannot pass through said
8 cell inlet when said inlet valve is closed; and,

9 (ii) a reagent inlet for inputting said reagent into said chamber, said reagent
10 inlet having a reagent valve in operable communication with said reagent inlet
11 for valving fluid flow through said reagent into said chamber, said inlet or said
12 chamber having an retention mechanism for retaining said cells in said

13 chamber while permitting flow of said reagent into said chamber when said
14 reagent valve is open;
15 wherein when said cells are loaded into said chamber, and said cell valve is
16 closed, said cells are retained in said chamber while said reagent valve is open
17 and closed;
18 (b) opening said cell inlet valve and introducing said cells into said chamber;
19 (c) closing said cell inlet valve;
20 (d) opening said reagent valve to introduce said reagent into said chamber; and,
21 (e) introducing said reagent into said chamber while retaining said cells inside of said
22 chamber thereby perfusing said cells with said reagent.

1 77. A method for treating a particle comprising the steps of:

- 2 (i) providing a microfluidic device comprising:
 - 3 (a) an input mechanism for introducing a fluid sample containing a
4 particle;
 - 5 (b) a microfluidic passage in fluid communication with said input
6 mechanism;
 - 7 (c) a positioning mechanism in fluid communication with said
8 microfluidic passage, said positioning mechanism for positioning said
9 particle in said microfluidic passage while contained in said fluid
10 sample;
 - 11 (d) a retention mechanism for retaining said particle upon being positioned
12 by said positioning means;
 - 13 (e) a treatment mechanism in communication with said retention
14 mechanism for selectively treating said particle to produce a treatment
15 response while being retained within said retention mechanism; and,
 - 16 (f) a measurement mechanism for measuring said treatment response, if
17 any, of said particle.
- 18 (ii) introducing said sample fluid containing said particle into said input
19 mechanism;
- 20 (iii) positioning said particle with said positioning mechanism so that said
21 particle is retainable by said retention mechanism;
- 22 (iv) retaining said particle with said retaining mechanism;
- 23 (v) exposing said particle to said treatment by said treatment mechanism;

(vi) measuring said treatment response caused directly or indirectly by said particle upon exposure to said treatment.

1 78. The method of claim 77 wherein said microfluidic device further comprises a release
2 mechanism for releasing said particle from said retention mechanism, and said method
3 further comprises the step of releasing said particle from said retaining mechanism.

1 79. The method of claim 78, wherein said microfluidic device further comprises an output
2 mechanism for outputting said particle from said microfluidic device, and said method further
3 comprises the step of outputting said particle from said microfluidic device by said output
4 mechanism.

1 80. The method of claim 78, wherein said microfluidic device further comprises a cell
2 culture mechanism for culturing said particle, and the method further comprises the step of
3 culturing said particle in said cell culture mechanism.

1 81. The method of claim 77, wherein said microfluidic device further comprises a control
2 mechanism for determining aspects of the flow rate or path of the sample fluid or other fluid,
3 and the method further comprises the step of determining the flow rate or path of the sample
4 fluid or other fluid by said control mechanism.

1 82. The method of claim 81, wherein said control mechanism is a valve in communication
2 with said microfluidic passage, and the method further comprises valving said sample fluid or
3 other fluid with said valve.

1 83. The microfluidic device of claim 82, wherein said microfluidic device is formed from
2 a multi-layer elastomeric block and, wherein said valve is formed from an elastomeric
3 membrane within said elastomeric block, and wherein said valving occurs by deflecting said
4 elastomeric membrane into said microfluidic passage.

1 84. The method of claim 82, wherein said control mechanism is a pump in
2 communication with said microfluidic passage, and wherein said determining the flow rate or
3 path of said sample fluid occurs by actuation of said pump.

1 85. The method of claim 84, wherein said microfluidic device is formed from a multi-
2 layer elastomeric block and, wherein said pump is formed from an elastomeric membrane

3 within said elastomeric block, and wherein said pump is actuated by deflecting a series of
4 elastomeric membranes into said microfluidic passage in a selected sequence.

1 86. The method of claim 77, wherein said microfluidic device comprises a multi-layered
2 elastomeric block having a control layer having an elastomeric membrane deflectable into
3 said microfluidic passage in a fluidic layer to selectively determine the flow rate or path of a
4 fluid in said microfluidic passage.

1 87. The method of claim 77, wherein said microfluidic passage further comprises an
2 adjacent passage joining said microfluidic passage at a junction or branch, said adjacent
3 passage being selected from the group consisting of inlet passage, outlet passage, particle
4 passage, reagent passage, and waste passage, and said method further comprises the step of
5 selectively determining the path of said particle to said adjacent passage.

1 88. The method of claim 87, wherein said adjacent passage is a dead-end passage, and
2 wherein said selectively determining includes introducing said sample fluid into said dead-
3 end passage wherein said sample fluid displaces gas, if present, in said dead-end passage to
4 fill said dead-end passage with said sample fluid.

1 89. The method of claim 87 further comprising said adjacent passage manipulating said
2 particle.

1 90. The method of claim 89, wherein said particle manipulating includes retaining said
2 particle in addition to either positioning, sorting, treating, detecting, propagating, storing,
3 mixing, or releasing said particle.

1 91. The method of claim 77, wherein said particle is selected from the group consisting of
2 cells, eukaryotic cells, prokaryotic cells, plant cells, animal cells, hybridoma cells, bacterial
3 cells, yeast cells, viruses, organelles, beads, and vesicles, and wherein said treating step treats
4 said particle.

1 92. The method of claim 91, wherein said particle is a plurality or an aggregate of
2 particles, and said method further comprises a sorting step to sort out and separate or isolate a
3 desired particle from said plurality of particles, and said treating step treats said separated or
4 isolated particle.

1 93. The method of claim 92, wherein said plurality of particles is a complex mixture
2 containing different particles, and said sorting step sorts out at least one type of particle from
3 other different particles in said complex mixture.

1 94. The method of claim 93, wherein said complex mixture containing different particles
2 is whole blood or serum or bodily fluid, and said sorting step selects for at least one type of
3 cell from the whole blood or serum.

1 95. The method of claim 77, wherein said particle is an egg or embryo, and said treatment
2 is a step towards in-vitro fertilizing or manipulating said egg or embryo, respectively.

96. The method of claim 77, wherein the input mechanism is a receptacle or well in fluid
communication with said microfluidic passage, and said method further comprises the step of
5 introducing said fluid sample into said receptacle.